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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/532,998

11/10/2005

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07430-00150-USU

1655

23416 7590 10/07/2008
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EXAMINER

NOAKES, SUZANNE MARIE

ART UNIT

PAPER NUMBER

1656

MAIL DATE

DELIVERY MODE

10/07/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/532,998	Applicant(s) KONSTANTINOV ET AL.	
	Examiner SUZANNE M. NOAKES	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 July 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 July 2008 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>04/30/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants are notified that the location and Examiner handling the instant Application has changed in the Office. Please note that all further correspondence should be sent to Art Unit 1656 and to the Examiner signed below.

Status of the Claims

2. The amendments filed 09 July 2008 are acknowledged. Claims 1-11 remaining pending and subject to examination.

Information Disclosure Statement

3. The IDS filed April 30, 2008 has been received and is signed and considered; a copy of the PTO 1449 is attached to the following document.

Withdrawal of Rejections/Objections

4. The objection to the Drawings, and specifically Figure 1, is withdrawn in view Applicants submission of a Replacement Drawing Sheet which removes the Figure legend.

5. The objection to the specification for use of the Trademark "Pluronic" is withdrawn in view of Applicants amendments to the specification.

6. The rejection of claim 7 under the second paragraph of 35 U.S.C. 112 for use of a Trademark in a claim is withdrawn in view of the amendment to said claim.

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7. The rejection of claims 1-11 under 35 U.S.C. 103(a) as being unpatentable over Rancke-Madsen et al., U.S. Patent No. 6,087,148 in view of Koch et al., U.S. Patent No. 6,143,331 and Schulz et al., 1997 is withdrawn upon further consideration by the Examiner and in consideration of Applicants arguments.

New Rejections/Objections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moller et al. (US 6103502 – cited on IDS of April 2008) in view of Schulz et al., 1997 (cited in the IDS filed 28 April 2005) and Palomares et al. (Enzymes and Microbial Technology, 2000 Mar 1;26(5-6):324-331).

Moller et al. teach a that the need to isolate a protein or peptide from fermentation medium typically arises in the context of recombinant microorganisms transformed with suitable expression vectors. Desired proteins or peptides, for the taught ultrafiltration process, are typically a recombinantly produced protein or peptide (see col. 1, lines 19-24). The method of concentrating a macromolecule of interest via ultrafiltration of a cell culture supernatant encompasses subjecting said cell culture supernatant (from a decanted culture medium – see col. 5, lines 4-7) wherein said first

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supernatant (e.g. retentate) is adjusted to have a conductivity of less than 6 mS/cm and is subjected to a first ultrafiltration process which is immediately followed by diafiltration (e.g. desalinization by addition of water) until the conductivity is adjusted to less than 2.2 mS/cm. This second retentate can then be subjected to a second concentration/ultrafiltration step (see col. 5, lines 7-48).

Moller et al., however, do not teach adding an organic nonionic block copolymer such as Pluronic F-68 to the cell culture mediums such as animal cell cultures or insect cell cultures.

Schulz et al. teach that ultrafiltration (UF) is one of the most efficient processes recommended as a first step in downstream procedures for the recovery of proteins from mammalian cell cultivation. Cell culture supernatants consist of a broad spectrum of compounds, which influence the performance of UF. These include supplements of the culture medium (e.g. Pluronic F-68, silicone oil) or compounds that are secreted from the cells or released after cell lysis (e.g. proteins, lipids). The nonionic block copolymer Pluronic F-68 is often supplemented in cell culture media for animal cells in order to protect the cells from shear stress caused by sparging. Figure 1 discloses the overall method wherein cell culture (either CHO cells +/- F-68 and SM1F6 cells +/- F-68 wherein the protein of interest is gp220/350 Epstein-Barr-Virus surface antigen) are processed through ultrafiltration and/or subsequently through diafiltration (see Figures 1 and also 5).

Palomares et al. teach the following (see p. 324, 1st column, 1st paragraph):

“Pluronic F-68 (PF68) has been widely used as a shear protective agent for animal cells in suspension culture. Its use has resulted in increased cell survival and cell concentration, particularly in cultures with serum-free media or in bioreactors where cells are subjected to deleterious shear stresses. The effectiveness of PF68 has been proven by many research groups in both mammalian and insect cell lines [1–14, reviewed in 15].”

Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to use/add Pluronic F-68 in the cell culture medium in the methods as taught by Moller et al. when said method is being used to cultivate animal or insect cells. While Moller et al. method is applicable to all cell culture supernatants (their primary example is from yeast), it is very well known that when cultivating animal and insect cells that the additive Pluronic F-68 (or similar block nonionic copolymers) *must* be added to the cell cultures in order to prevent the cells from essentially dieing in the fermentation process (and hence no production of the protein of interest is possible). For these reason, one skilled in the art would also be motivated to add said Pluronic F-68 to the cell culture medium, when said skilled artisan is cultivating animal or insect cells. There would be a significant expectation of success in performing Moller et al. methods of adjusting the conductivity of *any* cell culture supernatant (e.g. an aqueous starting material, inclusive of animal or insect cells) to less than 6.0 mS/cm, subjecting said supernatant to ultrafiltration followed by diafiltration to adjust the conductivity to less than 2.2 mS/cm (which is "about" 1.5 mS/cm) and then reconcentrate the second retentate by way of another ultrafiltration step because Schulz et al. explain that ultrafiltration and diafiltration are one of the most efficient processes recommended as a first step in downstream procedures for the recovery of proteins from mammalian cell cultivation and thus use of Pluronic F-68 is essential in this process and because

Palomares et al. teach that said Pluronic F-68 is also vital for insect cell cultures in an analogous manner to mammalian cell cultures.

Thus the claims are deemed to be *prima facie* obvious over the teachings of Moller et al. and in view of Schulz et al. and Palomares et al.

Response to Arguments

9. Applicant's arguments with respect the previous 35 U.S.C. 103(a) rejection as recited in the previous Office action (claims 1-11) have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUZANNE M. NOAKES whose telephone number is (571)272-2924. The examiner can normally be reached on 7.00 AM-3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Suzanne M. Noakes/
Examiner, Art Unit 1656
01 October 2008